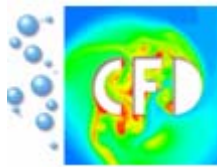


Numerical methods and CFD techniques for drug application in tumor treatment

Elena Shcherbinina

Supervisors: Prof. S.Turek (Dortmund), JProf.D.Kuzmin (Dortmund), Prof. P.Kloucek (Neuchatel)



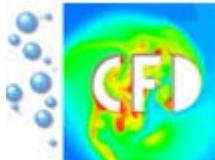
Introduction

- Motivation
- Schematic view

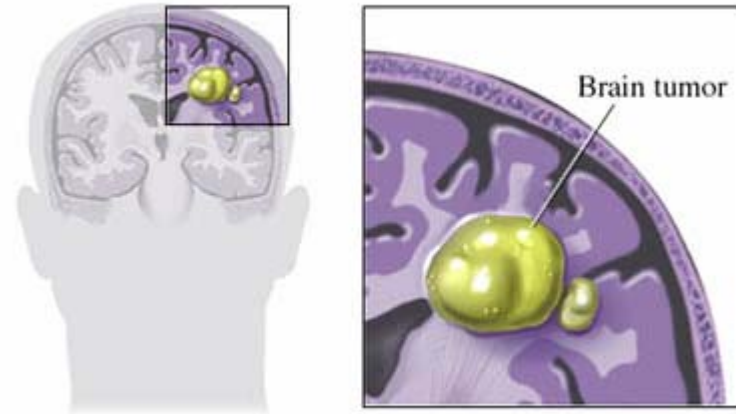
Mathematical model

- Equations
- Discretization
- Results

Summary



- Each year a lot of people in the world are diagnosed with a primary or metastatic tumor
- There are over 120 different types of brain tumors

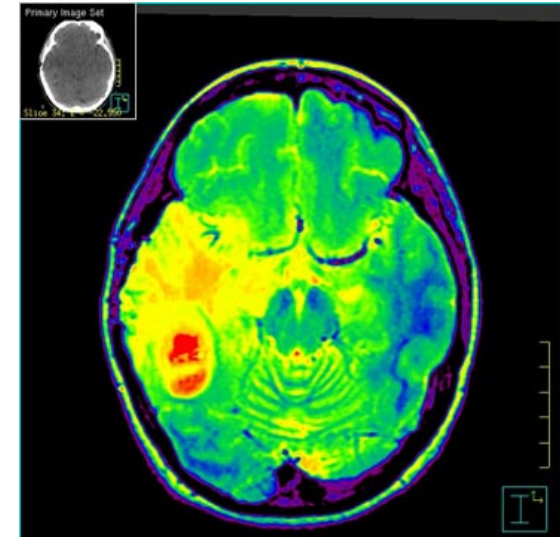


- application to drug delivery in brain tumors
- solution of derived partial differential equations (PDE's)
- use modern computational fluid dynamics (CFD) tools (Featflow)

There are two principal physiological barriers:

the blood-brain barrier (BBB)

- The BBB hinders the delivery of many potentially important diagnostic and therapeutic agents to the brain



the interstitial fluid pressure

- The interstitial fluid pressure is present within the tumor and reduces the driving force for fluid and solute to be extravasated into the brain tissues

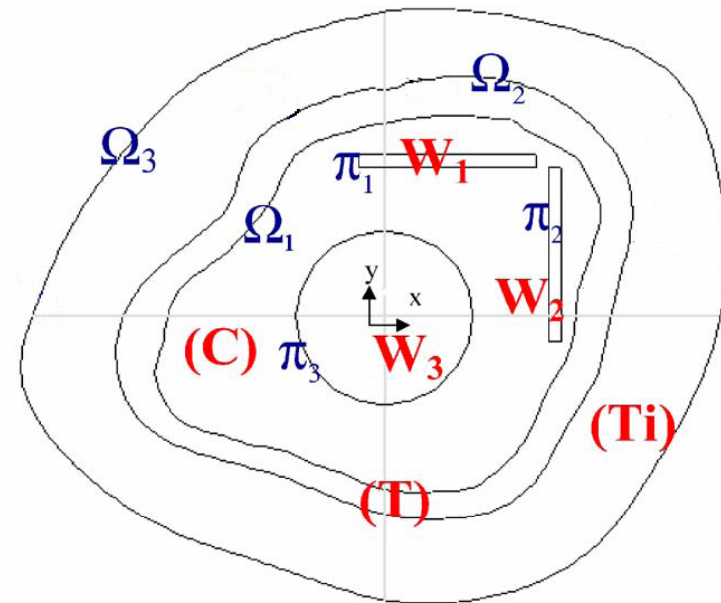
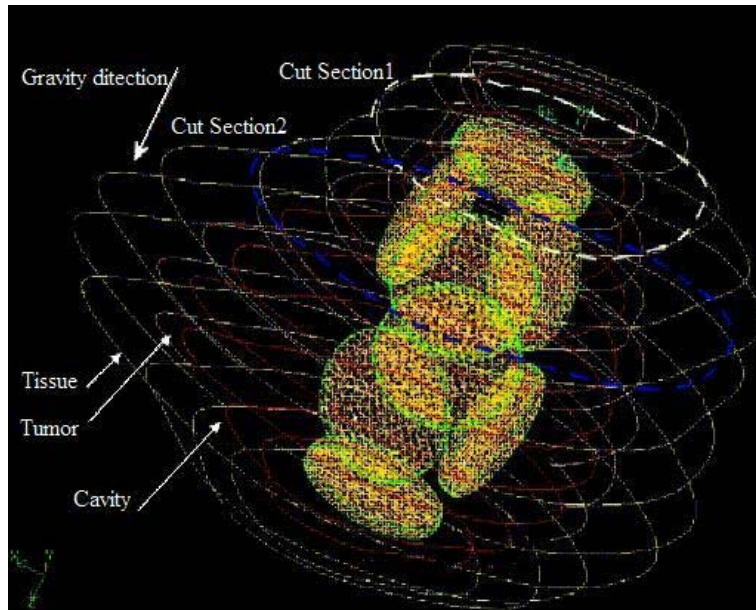


Fig.1: $W_{1,2,3}$ - wafers 1-3, (C) - the resection cavity after the surgery, (T) - the remnant tumor that are not removed in the surgery, (Ti) - the normal tissues surrounding the tumor, Ω_1 - boundary between cavity and tumor, Ω_2 - boundary between tumor and tissues, Ω_3 - external boundary, $\pi_{1,2,3}$ - boundaries cavity and wafers

The mass conservation equation

$$\nabla \cdot \vec{V} = \begin{cases} F_v - F_l + q & \text{in tumor (T) and normal tissues (Ti)} \\ 0 & \text{in cavity (C) and wafers (W}_{1,2,3}) \end{cases}$$

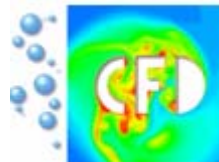
The momentum equation

$$\frac{\partial \rho \vec{V}}{\partial t} + \nabla \cdot (\rho \vec{V} \vec{V}) = \rho \vec{g} - \nabla P_i + [\nabla \cdot \mathbf{\Gamma}] + \Theta \mu \vec{V} + \frac{\rho}{2} \Psi |\vec{V}| \vec{V}$$

The drug concentration

$$\frac{\partial C}{\partial t} + \vec{V} \cdot \nabla C = D \Delta C - R + F_s - F_{ls}$$

(T.Lee, W. Tan, C.-H. Wang, 2004)



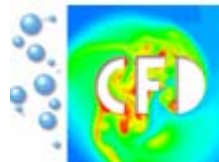
$$F_v = \frac{K_v S}{V} (P_v - P_i - \sigma_T (\pi_v - \pi_i)) \quad \text{Starlings law}$$

$$F_s = \begin{cases} S_0 e^{-t/\tau} & \text{in wafers } (W_{1,2,3}) \\ F_v (1 - \sigma) C_v + \frac{\pm S}{V} (C_v - C) \cdot \frac{Pe_v}{e^{Pe_v} - 1} & \text{in tumor (T) and tissues (Ti)} \\ 0 & \text{in cavity (C)} \end{cases}$$

$$R = \begin{cases} k_e C & \text{in cavity (C)} \\ \frac{V_{max} C}{K_m + C} + k_e C & \text{in tumor (T) and normal tissues (Ti)} \\ 0 & \text{elsewhere} \end{cases}$$

$$Pe_v = \frac{F_v (1 - \sigma)}{\pm S / V} \quad \text{Peclet number}$$

$$\pi_{i,v} = R \cdot T \cdot C_{i,v} \quad \text{Van Hoff /s law}$$



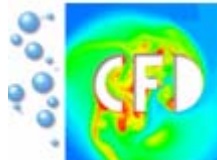
Abstract view of the dimensionless equations

$$\left\{ \begin{array}{l} \nabla \cdot \vec{V} - \tilde{k} \cdot P = 0 \\ \frac{\partial \vec{V}}{\partial t} + \nabla \cdot (\vec{V} \vec{V}) = \vec{g} - \nabla P_i + [\nabla \cdot \mathbf{\Gamma}] + \Theta \nu \vec{V} + \frac{1}{2} \Psi |\vec{V}| \vec{V} \\ \tilde{q} \cdot \frac{\partial C}{\partial T} + \tilde{d} \vec{V} \cdot \nabla C = \Delta C - \tilde{f} \cdot C \end{array} \right.$$



Discretized equations

$$\rightarrow \begin{bmatrix} A & B \\ B^T & -k \cdot I \end{bmatrix} \begin{bmatrix} \tilde{V} \\ P \end{bmatrix} = \begin{bmatrix} f \\ g \end{bmatrix}, \text{ where } \tilde{V} = (V, C)$$



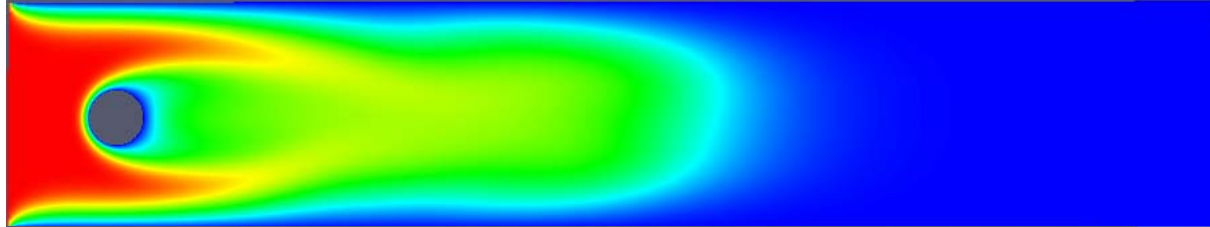
	Velocity/Pressure	Concentration
element	\tilde{Q}_1/Q_0	Q_1
solver	Multigrid	Umpack
grid	unstructured	unstructured

Results

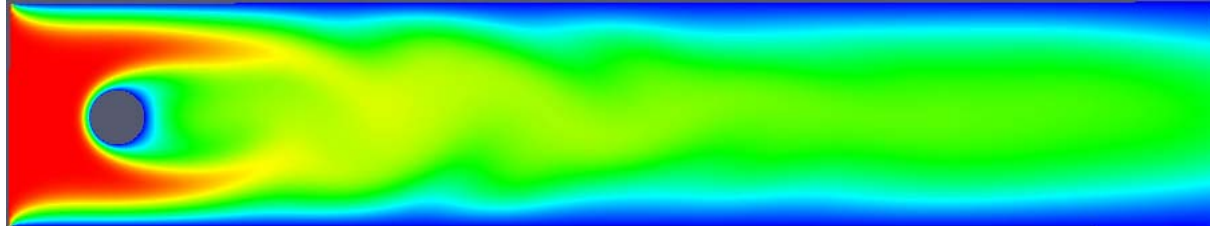
Time step = 001



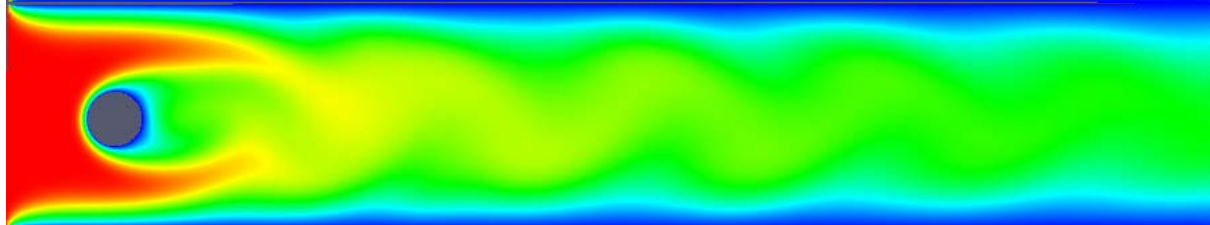
Time step = 050



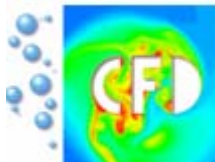
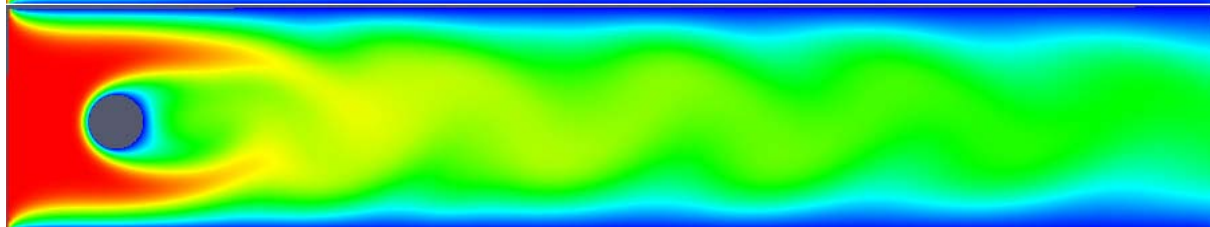
Time step = 100



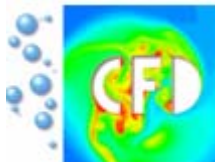
Time step = 150



Time step = 200



- closed system of PDE's for the velocity, pressure and drug concentration
- saddle-point problem requires techniques for incompressible flow problems
- the fully coupled problem
- numerics for CFD

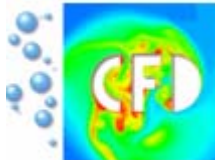


Thank you for your attention!!!

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μ -interstitial fluid viscosity

ρ -interstitial fluid density

Θ -matrix for viscous term

Γ -stress tensor

Ψ -matrix for inertial term

F_l -net gain fluid

F_v -net fluid loss

P_v -interstitial pressure

P_i -vascular pressure

π_v -osmotic pressure of plasma

R -reaction in the cavity

Pe_v -transcapillar Peclet number

F_s -drug gain from the blood capillaries

F_{ls} -drug loss to the lymphatic vessels

C -drug concentration

$N_{1,2,3}$ -outward normal vectors of $\Omega_{1,2,3}$

K_v -hydraulic conductivity

S/V -exchange area

π_i -osmotic pressure of interstitial fluid

σ_T -osmotic reflection coefficient